UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,959	08/26/2003	Choong-Chin Liew	4231/2032	7379

29933 7590 02/09/2007

PALMER & DODGE, LLP
KATHLEEN M. WILLIAMS
111 HUNTINGTON AVENUE
BOSTON, MA 02199

EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	PAPER NUMBER
1636	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/649,959	LIEW ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 12-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11 and 20-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/15/2005, 11/3/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 11/16/2006, in which claim 11 was amended, and claims 20-24 were newly added. Currently, claims 1-24 are pending.

Election/Restrictions

Applicant's election with traverse of Group III in the reply filed on 11/16/2006 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden on the Examiner to search the claims of elected Group III with each one or combination of the polynucleotides of Groups I and IV recited in Tables 2 and 3 since the searches overlap with each other, and on the grounds that it would not be an undue burden on the Examiner to search the claims of Group III with each one or combination of the polypeptides of Groups II and V recited in Tables 2 and 3 since the searches overlap with each other. This is not found persuasive because the searches of the polynucleotides of Groups I and IV or polypeptides of Groups II and V do not overlap with the search required for elected Group III. Group III does not require the search of any of the polynucleotides of Groups I and IV or polypeptides of Groups II and V. The method of Group III does not make or use the polynucleotides of Groups I & IV or the polypeptides of Groups II & V. In other words, the method of Group III is not related to the products of Groups I and II or methods of Groups IV and V for the reasons set forth on page 7 of the Office action mailed 5/16/2006. Each one or combination of the polynucleotides or polypeptides of Groups I, II, IV and V requires a separate search of the patent and non-patent literature that is not required for the search of Group III. Accordingly, the searches are not co-

extensive, and the additional searching required to search more than Group III would impose a serious search burden.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-10 and 12-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/16/2006.

New claims 20-24 read on the invention of elected Group III. An examination on the merits of claims 11 and 20-24 follows.

Information Disclosure Statement

Receipt of information disclosure statements, filed on 11/3/2003 and 9/15/2005, is acknowledged. The signed and initialed PTO 1449s have been mailed with this action.

Specification

The attempt to incorporate subject matter into this application by reference to an embedded hyperlink is ineffective. Hyperlinks are found at page 52, line 12 and page 53, line 18 of the specification. The specification attempts to incorporate protocols available at a web site by reference to the abovementioned hyperlinks. The attempt to incorporate subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See 37 CFR 1.57(d) and MPEP §

608.01(p), paragraph I regarding incorporation by reference. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The use of the trademarks TEXAS RED (page 23, line 19), CY3 (page 13, line 16; page 23, line 19; page 52, lines 7 and 14; page 53, lines 2, 5, 8, 13 and 14; page 56, lines 20 and 27), CY5 (page 13, line 16; page 23, line 19; page 52, lines 7 and 14; page 53, lines 2, 5, 8, 13 and 14; page 56, lines 20 and 27), TRIZOL (page 48, line 11; page 52, line 5; page 59, line 15), MEGASCRIPT (page 52, line 4), GENBANK (page 14, lines 15 and 16), and UNIGENE (page 14, line 15; Table 2 heading; Table 3 heading) has been noted in this application. Trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The disclosure is objected to because of the following informalities: the word GENBANK is misspelled at pages 62 and 63 as "Gene Bank" and "GeneBank," respectively. The specification clearly indicates that Tables 2 and 3 refer to GENBANK Accession Numbers (e.g. page 14, lines 12-19). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11 and 20-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is vague and indefinite in that the metes and bounds of the phrase "with beta2-microglobulin" are unclear. The claim is drawn to the step of "contacting chondrocytes with beta2-microglobulin in the presence of a candidate modulator and in an absence of said candidate modulator." While the specification envisions the addition of beta2-microglobulin (B2M) to the chondrocyte culture at a concentration of 10 μg/ml, 20 μg/ml, or 30 μg/ml (e.g. Example 9 at page 58), it was known in the art at the time the invention was made that chondrocytes express B2M. Dell'Accio et al (Arthritis & Rheumatism, Vol. 44, No. 7, pages 1608-1619, July 2001) teach that B2M is a housekeeping gene expressed in primary human chondrocytes (e.g., page 1613, left column; Figure 2). Thus, primary human chondrocytes are "chondrocytes with beta2-microglobulin," as they normally express this protein regardless of whether the protein is added to the cell culture. Accordingly, it is unclear whether the step of contacting requires the addition of B2M protein to the culture or whether the step only requires contacting chondrocytes in the presence and absence of a candidate inhibitor. It would be remedial to amend the claim language to clearly indicate that beta2-microglobulin protein (i.e., gene product) is added to the culture comprising chondrocytes.

Claims 20-24 depend from claim 11 and thus are indefinite for the same reasons as applied to claim 11.

The term "chondrocytes are derived from" in claim 20 renders the claim indefinite. The term "derived from " is not defined by the claim, the specification does not provide a standard for

ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The term "chondrocytes are derived from" is unclear in that one of ordinary skill in the art would not know how much one could vary the chondrocytes in terms of differentiation state (e.g., de-differentiation), for example, and meet the limitations of the claimed invention.

The term "chondrocytes are derived from" in claim 21 renders the claim indefinite. The term "derived from " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The term "chondrocytes are derived from" is unclear in that one of ordinary skill in the art would not know how much one could vary the chondrocytes in terms of differentiation state (e.g., de-differentiation), for example, and meet the limitations of the claimed invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11 and 20-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying an inhibitor of beta2-microglobulin, said method comprising a) culturing chondrocytes without serum but with beta2-microglobulin protein, b) contacting the cultured chondrocytes in a presence of a putative modulator and in an absence of said putative modulator, and c) comparing the proliferation of said chondrocytes in said presence relative to said absence of said putative modulator, wherein a

specific increase in the proliferation of said chondrocytes in said presence relative to said absence of said putative modulator identifies said putative modulator as said inhibitor of said activity of said beta2-microglobulin, does not reasonably provide enablement for embodiments where beta2-microglobulin protein is not specifically added to the culture in the absence of serum or embodiments where the putative modulator must be a known modulator (i.e., a "candidate modulator"). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The claims are drawn to a method of identifying an inhibitor of an activity of beta2-microglobulin (B2M), said method comprising the steps of a) contacting chondrocytes with B2M in a presence and in an absence of a candidate modulator, and b) comparing the proliferation of the chondrocytes in the presence relative to the absence of the candidate modulator, where a specific increase in the proliferation of the chondrocytes in the presence of the candidate modulator relative to the absence of the candidate modulator identifies the candidate modulator as an inhibitor of B2M activity. The dependent claims further limit the chondrocytes used in the method to chondrocytes from a subject with osteoarthritis (claim 20),

chondrocytes from a subject with severe osteoarthritis (claim 21), primary chondrocytes (claim 22), cultured chondrocytes (claim 23), and human chondrocytes (claim 24).

The instant specification defines the term "candidate modulator" to mean a molecule that is capable of modulating (i.e., increasing or decreasing) the activity of B2M or the B2M related genes or gene products (page 24, lines 1-3). With respect to the claimed invention, the candidate modulator must be a molecule that is capable of decreasing, or inhibiting, the activity of B2M. Thus, one must know which structures are capable of performing this function, such that one could make and use the compounds prior to the application of the compounds within the context of the claimed method.

Even if one could make a "candidate modulator," the nature of the invention is complex in that chondrocytes express B2M. Dell'Accio et al (Arthritis & Rheumatism, Vol. 44, No. 7, pages 1608-1619, July 2001) teach that B2M is a housekeeping gene expressed in primary human chondrocytes (e.g., page 1613, left column; Figure 2). Thus, primary human chondrocytes are "chondrocytes with beta2-microglobulin," as they normally express this protein regardless of whether the protein is added to the cell culture. Thus, one must be capable of using the claimed method where chondrocytes are contacted in the presence of a candidate modulator and an absence of the candidate modulator, and chondrocyte proliferation is compared between the two groups such that an increase in proliferation in response to the candidate modulator identifies the candidate modulator as an inhibitor of B2M activity.

Breadth of the claims: The claims are broad in that they do not specifically require the use of B2M protein in the method, yet the intent of the method is to identify inhibitors of B2M

protein activity. The complex nature of the subject matter of this invention is exacerbated by the breadth of the claims.

Guidance of the specification and existence of working examples: The specification teaches that B2M mRNA is expressed in human fetal cartilage samples, as well as adult human normal, mild osteoarthritis (OA), and severe OA cartilage samples (e.g., page 54, lines 1-9). At the time the invention was made, the effect of exogenous B2M protein on chondrocyte proliferation was not known (e.g., page 55, lines 10-16). To investigate whether B2M has any effect on chondrocyte proliferation, Applicants cultured human severe OA chondrocytes with increasing concentrations of B2M in media with or without fetal calf serum (FCS) for 48 hrs (e.g., page 55, lines 17-24). After culturing the chondrocytes in the presence of B2M for 48 hrs, proliferation of the chondrocytes was determined by their ability to cleave WST-1, which is reflected as the absorbance at 450 nm (e.g., page 55, lines 17-24). B2M did not have a significant effect on the proliferation of the chondrocytes in the presence of FCS (e.g., page 55, lines 17-24). In contrast, B2M inhibited the proliferation of chondrocytes in the absence of FCS, where the inhibition was significant at a B2M concentration of 10 μg/ml (e.g., page 55, lines 17-24; Figure 4).

The specification envisions performing an assay to identify inhibitors of an activity of B2M activity, which refers to the ability of a candidate modulator to specifically inhibit the function or the expression of the B2M gene or gene product, where the normal function of B2M is to inhibit chondrocyte proliferation (e.g., paragraph bridging pages 30-31). The specification envisions the identification of inhibitors of B2M related activity by their ability to increase chondrocyte proliferation in the presence of B2M protein (e.g. page 45, lines 15-18; Example 9).

The specification does not provide any working examples where any "candidate modulator" is shown to inhibit a B2M activity. A prophetic example, Example 9, describes an *in vitro* assay for the identification of inhibitors. The prophetic example sets forth the following method steps: (i) isolating human chondrocytes from normal or severe OA patients, (ii) seeding the chondrocytes at $1x10^4$ cells/well in triplicate into a 96 well plate, (iii) culturing the cells without FCS but with 10 μg/ml, 20 μg/ml, and 30 μg/ml of B2M along with the putative inhibitor in concentrations of 0.1 μg/ml, 1 μg/ml, or 10 μg/ml for 48 hours, (iv) measuring chondrocyte proliferation by adding 10 μl of WST-1 to each well and scanning the plate with a microplate reader at an absorbance of 450 nm, and (v) comparing the readings of wells wherein chondrocytes are incubated with B2M along with the putative inhibitor are compared with wells wherein chondrocytes are incubated with B2M alone (e.g. page 58, lines 14-26). Unlike the instant claims, this method requires the addition of a "putative modulator" rather than a "candidate modulator," which the specification defines as a molecule that is capable of modulating (i.e., increasing or decreasing) the activity of B2M or the B2M related genes or gene products (page 24, lines 1-3). With respect to the claimed invention, the candidate modulator must be a molecule that is known to be capable of decreasing the activity of B2M. Thus, one must know which structures are capable of performing this function, prior to the application of the compounds within the context of the claimed method. The specification does not teach any *in vivo* screening assays.

With respect to "candidate modulators" the specification does not teach any specific examples of compounds that are capable of inhibiting the activity of B2M. The specification envisions the use of variants of B2M, B2M mimetics, antibodies to B2M, antisense RNA,

antisense DNA, ribozymes, RNAi, and non-steroidal compounds (e.g., page 31, line 16 to page 41, line 18; page 23, lines 20-23; page 30, lines 18-20). The specification does not provide specific guidance with regard to the chemical structure required for inhibitory function. Thus, one would not know how to make and use a "candidate modulator" for use in the claimed invention.

Predictability and state of the art: Around the time the invention was made, the effect of B2M on chondrocyte proliferation was not known (Moe and Chen. Seminars in Dialysis, Vol. 14, No. 2, pages 127-130, (March-April) 2001; e.g., page 129, left column, 2nd full paragraph). The instant specification teaches that B2M decreases chondrocyte proliferation, which contrasts with the ability of B2M to stimulate the proliferation of osteoblasts and the lack of effect of B2M on synovial fibroblast proliferation (e.g., specification, page 55, lines 10-16). The lack of recognition of B2M anti-proliferative activity upon chondrocytes around the time the invention was made, suggests that the area of the invention, including B2M inhibitors specific for increasing chondrocyte proliferation, were underdeveloped at the time the invention was made. Thus, it would be unpredictable to practice the claimed invention without specific guidance directed to how to make and use a "candidate modulator."

Even if the claimed method did not require one to know the structure of a modulator prior to performing the assay (i.e., a putative modulator was used in place of the claimed candidate modulator), it would be unpredictable to practice the invention as claimed. The instant specification teaches that B2M does not have a significant effect on the proliferation of chondrocytes in the presence of FCS (e.g., page 55, lines 17-24). Therefore, it would be unpredictable to practice the invention with chondrocytes cultured in the presence of FCS, or

serum in general. Moreover, it would be unpredictable to practice the invention without the addition of B2M protein to the medium of the cultured chondrocytes. If chondrocytes were contacted in the presence and absence of a putative modulator, and proliferation of the chondrocytes increased in the presence of the putative modulator, one would not be able to specifically attribute the increase in proliferation to inhibition of B2M activity. For example, Wohlrab et al (Biorheology, Vol. 39, No. 1-2, pages 55-61, 2002) teach that the addition of Na^+ ion channel and K^+ ion channel inhibitors, such as 4-aminopyridine and lidocaine, to human primary chondrocytes results in a temporary increase in chondrocyte proliferation (e.g. page 56, section 2.1; page 57, section 2.4; paragraph bridging pages 60-61; Figure 4). Therefore it would be unpredictable to attribute any compound-induced increase in the proliferation of chondrocytes to the inhibition of B2M activity.

Amount of experimentation necessary: The quantity of experimentation required to make and use the claimed invention is large. Given the lack of guidance in the specification with regard to the structure of the compounds capable of inhibiting B2M inhibition of chondrocyte proliferation, one would be required to perform a large amount of trial and error experimentation to identify compounds capable of inhibiting B2M. The claims encompass a genus of candidate modulators defined only by their function, where the relationship between the structural features of the members of the genus and the function have not been defined in the specification. In the absence of such a relationship, either disclosed in the instant specification or which would have been recognized based upon information readily available to one skilled in the art, the skilled artisan would not know how to make and use compounds that lack structural definition. The fact that one could have assayed a compound of interest using the disclosed assay does not overcome

this defect since one would have no knowledge beforehand as to whether or not any given compound would fall within the scope of what is claimed. It would require undue experimentation to randomly screen undefined compounds for the claimed activity. Even if the method did not require the use of a known modulator, one would not necessarily obtain inhibitors of B2M activity by performing the claimed method steps. As shown by Wohlrab et al (*supra*), contacting chondrocytes in the presence and absence of a compound may identify inhibitors of proteins such as ion channels rather than B2M. Thus, one would be required to perform additional experimentation to determine whether the compounds capable of increasing proliferation in the claimed assay are acting specifically upon B2M inhibition of chondrocyte proliferation rather than a non-B2M pathway. Accordingly, a large amount of inventive effort is required to be able to make and use the claimed method.

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed method. Therefore, claims 11 and 20-24 are not considered to be fully enabled by the instant specification.

Claims 11 and 20-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims encompass the provision of a genus of "candidate modulators" for use in the claimed method. The specification defines the term "candidate modulator" to mean a molecule that is capable of modulating (i.e., increasing or decreasing) the activity of beta2-microglobulin (B2M) or the B2M related genes or gene products (page 24, lines 1-3). With respect to the claimed invention, the candidate modulator must be a molecule that is capable of decreasing the activity of B2M. Thus, one must know which structures are capable of performing this function, prior to the application of the compounds within the context of the claimed method.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification envisions using molecules such as variants of B2M, B2M mimetics, antibodies to B2M, antisense RNA, antisense DNA, ribozymes, RNAi, and non-steroidal compounds as inhibitors (e.g., page 31, line 16 to page 41, line 18; page 23, lines 20-23; page 30, lines 18-20). The specification does not provide specific guidance with regard to the chemical structure required for inhibitory function. No compounds identified by the claimed assay are provided in the instant specification. Furthermore, there is no art of record that describes any B2M inhibitor. The relationship between the structural features of the members of the genus and the function have not been defined in the specification. Thus, it is impossible for one to extrapolate a specific chemical structure from the desired function and the provision of a generic class of molecule (e.g., RNA, DNA, protein, antibody, etc.) such that the compound would necessarily meet the structural/functional characteristics of the rejected claims.

For the written description requirement, an applicant's specification must reasonably convey to those skilled in the art that the applicant was in possession of the claimed invention as of the date of invention. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of candidate modulators, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

Given the very large genus of candidate modulators encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to the specific chemical structure of even one candidate modulator, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus of candidate modulators. Thus, there is no structural/functional basis provided by the prior art or instant specification for one of

skill in the art to envision those candidate modulators that satisfy the functional limitations of the claims. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention for claims 11 and 20-24.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

jad